

GENE POLYMORPHISMS AND RELATED CELL MARKERS IN PERIODONTITIS LESIONS

Akademisk avhandling

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av

Mauro Donati

Leg. tandläkare

Fakultetsopponent:

Professor **Bruno Loos**

Academic Center for Dentistry, Department of Periodontology, Amsterdam, Nederländerna

Avhandlingen baseras på följande delarbeten:

- I. Berglundh T, Donati M, Hahn-Zoric M, Hanson LÅ, Padyukov L. (2003) Association of the -1087 *IL-10* gene polymorphism with severe chronic periodontitis in Swedish Caucasians. *Journal of Clinical Periodontology* **30**: 249-254.
- II. Donati M, Berglundh T, Hytönen AM, Hahn-Zoric M, Hanson LÅ, Padyukov L. (2005) Association of the -159 CD14 polymorphism and lack of association of the -308 TNFA and Q551R IL-4RA polymorphisms with severe chronic periodontitis in Swedish Caucasians. *Journal of Clinical Periodontology* **32**: 474-479
- III. Donati M, Liljenberg B, Padyukov L, Berglundh T. (2008) Local expression of interleukin-10 and mCD14 in relation to the -1087 *IL-10* and -159 CD14 gene polymorphisms in chronic periodontitis. *Journal of Periodontology* **79**: 517-524
- IV. Donati M, Liljenberg B, Zitzmann NU, Berglundh T. (2009) B-1a cells and plasma cells in periodontitis lesions. *Journal of Periodontal Research* (Accepted for publication)
- V. Donati M, Liljenberg B, Zitzmann NU, Berglundh T. (2009) B-1a cells in experimental gingivitis in man. *Journal of Periodontology* (Accepted for publication)



Abstract

Gene polymorphisms and related cell markers in periodontitis lesions

Mauro Donati

Inflammatory and immune reactions to microbial plaque are the predominant features of periodontitis. Epidemiological studies revealed that differences in periodontitis among individuals could not be explained by differences in oral hygiene alone and that not everybody is equally susceptible. Periodontitis is considered to be a multifactorial disease where the interaction of multiple genetic and environmental components results into disease expression. The objectives of the present series of studies were (i) to investigate the association of gene polymorphisms related to some immune regulation components (*IL10*, *TNFA*, *IL4RA* *CD14*) with severe chronic periodontitis (studies I-II), (ii) to study the local expression of some immune regulation components in relation to gene polymorphisms in subjects with chronic periodontitis (study III), (iii) to study the correlation between inflammatory cells and functional markers in gingival lesions obtained from subjects with severe chronic periodontitis (study IV) (iv) and to study the reaction of B-1a cells to *de novo* plaque formation in subjects who were treated for severe chronic periodontitis (study V).

It was demonstrated that the proportion of subjects that exhibited the -1087 *IL10* GG genotype was significantly larger in the group with severe periodontitis than in the group of healthy controls (study I), that the proportion of subjects that exhibited the -159 *CD14* TT genotype was significantly smaller in the group of subjects with severe periodontitis than in the periodontally healthy group (study II) and that the proportion of IL-10 positive cells in the peripheral area of periodontitis lesions was significantly larger in subjects with the -1087 *IL10* GG genotype than in subjects with AG or AA genotypes (study III).

It was also observed that B cells (B-1a cells and B-2 cells) occurred in larger proportions than T cells, plasma cells and neutrophils in periodontitis lesions and a significant correlation was found between percentages of B-1a cells and plasma cells and between densities of B-lymphocytes and plasma cells (study IV). Further, biopsies retrieved after 3 weeks of plaque accumulation contained larger proportions of B-1a cells than biopsies representing healthy sites (study V).

Key words: Allele, B-lymphocyte, cell-surface molecule, cytokine, gene expression, genotype, gingivitis, host response, inflammation, periodontal disease

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Correspondence: Mauro Donati, Department of Periodontology, Institute of Odontology, The Sahlgrenska Academy at University of Gothenburg, Box 450, SE 405 30 Göteborg, Sweden.

E-mail: mauro.donati@odontologi.gu.se